

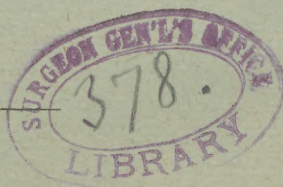
Bowen, (John T.)

ON THE OCCURRENCE
OF
SMALL-POX LESIONS IN THE
INTERNAL ORGANS,

WITH
SOME STUDIES OF THE SKIN ERUPTION,

BY JOHN T. BOWEN, M.D.,
BOSTON.

(Translated and reprinted from the "Vierteljahresschrift für Dermatologie und Syphilis," 1887. 4 Heft 1 Hälfte.)



BOSTON:
PRESS OF ROCKWELL AND CHURCHILL,
No. 39 ARCH STREET.
1888.

With the writer's compliments.

From Professor Weichselbaum's laboratory in Vienna.

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WHILE it is well known that small-pox causes efflorescences not only upon the skin, but also upon the mucous membranes, very few observations on the existence of analogous lesions in the internal organs have been recorded. Wagner described certain changes in the testicles, which will be again referred to, as well as "Lymphomknötchen," but these appearances are evidently not to be regarded as specific products of small-pox, as they occur in other infectious diseases. Weigert described small foci, seen only microscopically, in the liver, spleen, lymphatic glands, and kidney, which were characterized by the fact that the cell nuclei in the affected area could be only partially or not at all stained, while in the centre small blood-vessels, filled with colonies of micrococci, were to be seen. While these appearances could be detected only under the microscope, Weigert¹ found in one case of variola in an advanced stage, foci in the liver which could be distinguished with

¹ Anatomische Beiträge zur Lehre von den Pocken. II. Theil. 1875.

the naked eye, although still of miliary size. Each of these foci also showed microscopically a colony of bacteria in the centre, situated usually within a blood-vessel, and surrounding it, irregular, clustered masses of a faintly-glistening appearance, together with small, deeply-stained nuclei. The largest of these nuclei were as large as those of the white blood globules in the vicinity. Besides these, a detritus, composed of coarse and fine, deeply stained granules, was detected. The peripheral part of these foci consisted of opaque liver cells without nuclei, between which were observed cells in greater or less numbers, which were exactly similar to the white corpuscles of the blood. Around these foci there could often be seen a broad, clear areola, apparently empty or else filled with a clear fluid. This areola contained no liver cells, but was infiltrated with radiating fibrils, which extended into the blood-vessels of the liver, and which were partially covered with white blood corpuscles.

As to the nature of these foci, they are regarded by Weigert as analogous to the skin efflorescences of variola, as he found in them the same histological appearances that he could demonstrate in the skin lesion. That is to say, he had described as especially characteristic of the skin efflorescence, a peculiar form of necrosis in the lower layers of the rete Malpighii, which consists in a change of the rete cells into irregular masses, in which no nuclei can be differentiated by staining. This kind of degeneration was named by Weigert a *diphtheroid* necrosis, on account of its similarity to that form of necrosis described by Wagner as occurring in diphtheria; moreover, he considered it to be the primary and specific result of the action of the small-pox poison, regarding all the remaining changes in the epidermis as secondary and the result of irritation. Among these secondary manifestations, he included the formation of a network in the efflorescence, which he explains by the pressing in of the lymph into the dead epidermal cells, and by its coagulation. Also the proliferation of the epidermal cells, the formation of the umbilication, and the appearance of suppuration, are regarded as secondary manifestations. Finally, he called attention to the frequent appearance of bacteria, namely, micrococci, in the lymph or blood-vessels in the area of the lesion.

¹Anatomische Beiträge zur Lehre von den Pocken. I. Heft. 1874.

Weigert traces a resemblance between the foci in the internal organs and the efflorescences on the skin, chiefly from the presence of a necrosis in the former, which does not lead to the formation of a network, because in the foci in the internal organs the lymph can press in *between* the cells. Per contra, in the epidermis, on account of the much closer connection between the cells, the lymph must spread out *within* the cells, which then assume partly the form of a network, partly that of irregular masses.

The fact that no cell proliferation was found in the necrotic foci in the internal organs is not, in Weigert's eyes, opposed to the assumed analogy with the skin efflorescences, as nothing is known of the possibility of a replacement of dead cells by new epithelial elements in the liver and kidneys; and, at all events, the rete is physiologically much better suited to the formation of new cells than the organs in question. Further, an indication of a replacement of the dead cells was found in at least one case in the foci in the liver.

The appearance of pus corpuscles was also detected, according to Weigert, especially in the case where miliary foci were found in the liver. Here the foci were in great part infiltrated with pus corpuscles, and also surrounded by an areola, which gave the impression of a beginning sequestration.

Finally, micrococci were found in these foci, situated in the blood-vessels, and were regarded by Weigert as the cause of the necrosis. Weigert, therefore, concludes from this evidence, that the non-nucleated foci found by him in the internal organs in small-pox, are to be regarded at least as similar to the skin lesions.

Attention has recently been directed by Chiari¹ to certain changes in the testicles in variola, which had already been observed by other authors (Beraud, Laboulbène, Wagner), but had been almost entirely forgotten. Chiari had an opportunity to examine the testicles in fifteen cases of small-pox, mostly in children, and found in them constantly definite pathological appearances, viz., small, nodular foci. In one patient quite well of variola, and in nine cases in stadio exsiccationis, they were detected, as a rule, at the first cut, and sometimes they could be felt from the exterior as moderately hard nodules. They were characterized by a yellowish color and cheesy appearance.

¹ Zeitschrift für Heilkunde. Bd. vii. 1886.

Of five cases in stadio floritionis, four in children exhibited foci, from the size of a pin's head to that of a hemp-seed, of a grayish yellow color, often combined with extravasation, and less sharply defined than in the previous cases. In the fifth case (a man 43 years of age), the foci were so small that they could not be detected until the sections were stained.

Microscopically, the foci from the cases in the early stage of the disease showed in places a swelling and small-celled infiltration of the connective tissue, with a necrosis of all the cells lying in this connective tissue. The epithelium lining the seminal tubules was in this stage scarcely or not at all affected. In the cases where the process had lasted longer, the necrosis in the centre of these foci was already more extended, and the epithelium of the seminal tubules in this area completely necrotic; the zone of small-celled infiltration extended farther toward the periphery, and was more sharply bounded from the central zone of necrosis. In the cases of longest duration three zones could be seen: a central necrotic zone, a second zone of small-celled infiltration, and a third zone named the exudation zone. The connective tissue in this exudation zone appeared to be infiltrated with a finely fibrillar and finely granular coagulated exudation, which had pressed apart the pale, swollen, connective tissue cells. The epithelium of the seminal tubules in this zone was not affected by the staining agents. In the cases of shorter duration, this third zone was merely suggested. Micrococci were detected in two cases, situated in the blood-vessels.

These changes were regarded by Chiari as analogous to the diphtheroid necrosis in the epidermis in variola, and to the foci found by Weigert in the internal organs; and he is led to conclude from his investigations that the testicles, at least in the case of children, are almost constantly the seat of changes, seen usually with the naked eye, which are analogous to the lesions of the skin.

The above extracts from the literature show that observations on the appearance of lesions in the internal organs in small-pox similar to those upon the skin, are as yet very few in number, and that their significance is also somewhat doubtful. It seems proper, therefore, to record the following case (the material of which was kindly placed at my disposal by Professor Weichselbaum), and in addition to detail the results of some investigations of the testicles and skin in small-pox subjects.

CASE.—A woman, while suffering from confluent small-pox, gave birth to a female child in the small-pox department of the Rudolph Hospital in Vienna. The child was taken to the foundling asylum immediately after birth, but fourteen days later was brought back to the small-pox department of the Rudolph Hospital, ill with small-pox, where it died in four days.

Autopsy, three hours post-mortem. On the scalp four large pustules, one and a half centimeters in diameter, with a well-marked central depression; besides these, a smaller pustule about the size of a hemp-seed. On the trunk and extremities a few scattered pustules (perhaps ten or twelve), with their centres somewhat crusted. In the left pleural cavity, a thin, sero-fibrinous exudation, of a reddish color. The lower lobe of the right lung solidified, slightly granular, and almost non-crepitant. In the fluid from the cut surface of this lobe numerous micrococci, arranged in pairs and also in short chains, were to be seen in cover glass preparations.

In both lungs a number of nodules, from the size of a millet-seed to that of a hemp-seed, situated as a rule near the surface, dark red in the centre, with a gray periphery, and moderately firm. The centre of the nodules situated on the surface was depressed.

In both kidneys, especially in the cortex, were nodules similar to those in the lungs, but here they were as a rule somewhat smaller, *i.e.*, the size of a millet-seed. These nodules also were dark red in the centre, and a distinct umbilication was seen in those situated near the surface of the organ.

In the liver, especially near the surface, were pretty numerous gray nodules, moderately firm, which looked like miliary tubercles.

No nodules or other pathological appearances were found in the other organs.

During the autopsy, cultures were prepared from a pustule of the skin, from a nodule of the liver, from the pneumonia, and from the pleuritic exudation. The *Streptococcus pyogenes* developed in the form of a pure culture in all cases. In the cultures from the pustule of the skin there appeared on agar-agar plate cultures, other colonies besides the *Streptococcus pyogenes*, which proved, however, not to be pathogenetic.

As the macroscopic appearance of the nodules did not entirely exclude the possibility that they were of syphilitic origin, careful search was made for other manifestations of syphilis in the body, but without success. The epiphyses of the bones of the extremities were intact. No symptoms of syphilis could be discovered in the mother of the child, and no specific history could be obtained from the father.

The organs were hardened in absolute alcohol, numerous pieces imbedded in celloidine, and cut in serial sections according to Weigert's method. The sections were stained partly in alum carmine, partly in hæmatoxylon, or in hæmatoxylon-eosine. The microscopic examination yielded the following results:—

LIVER.—After the sections were stained many nodules were seen, which had not been detected before on account of their small size, and which were now distinguished from the surrounding tissue by their dark color. They were very numerous, so that several could be detected in each section.

Microscopically, every nodule was seen to consist of three zones, *i.e.*, a central necrotic portion, which was only slightly stained; a second zone, composed of small round cells and granular detritus, very deeply stained, and finally, a third or outer zone, which was less deeply stained, and gradually lost itself in the surrounding liver tissue. (Fig. 1, a, b, and c.)

After staining, the three zones could be distinguished with the naked eye alone.

The minute structure of the nodules was as follows: In all of the larger, but also in many of the smaller, nodules, the *central* zone contained a well-defined, irregular network, consisting of trabeculæ of varying thickness, which offered great similarity to the network seen in small-pox pustules of the skin, with the exception that it was somewhat finer. It consisted, like the latter, of trabeculæ and fibrils of varying thickness, and of irregular amorphous masses, which were only slightly stained by hæmatoxylon, took on a flesh-colored tint with alum carmine, and on double staining with hæmatoxylon-eosine, exhibited only the eosine color. No nuclei could be seen in the trabeculæ and fibrils, while in the interstices of the network lay an occasional nucleus, either apparently unaltered and well stained, or already in a state of granular degeneration, or else slightly or not at all stained. The net-

work appeared to be formed from necrotic cells, as Weigert has demonstrated for the network of the skin lesion, from the fact that in places a direct connection between the broad trabeculæ and the necrotic cells could be made out.

From serial sections it was learned that the network was most prominent in the centre of the nodules, although in many of the larger ones it could be traced nearly to the periphery; it was limited strictly to the centre only in the smaller nodules.

The central zone was always sharply bounded from the *second* zone, although the boundary line in the larger nodules was by no means regular, but more or less zigzag. This second zone consisted of small round cells, closely packed together and deeply stained, and lying between them, granules still smaller in size and also deeply stained, which were evidently derived from a disintegration of the round cells. No normal liver tissue could be seen in this zone. This zone was of varying width, and was not sharply bounded from the following zone.

The *third* zone consisted of cells pretty closely aggregated, the greater number of which were larger than those of the middle zone, and possessed either a rounded, or more irregular, sometimes flattened form. The nuclei were less deeply stained than those of the second zone. They were evidently spherical in form, containing one or two large nucleoli, and were frequently elongated or constricted, or in process of division. Besides these large forms, which suggested epithelium or endothelium, there were small, round cells, with nuclei composed of two or three divisions. They became more numerous toward the second zone, and at this point also small, deeply stained granules were occasionally seen between the cells. In many of the preparations, in addition to these appearances, a very fine, fibrillar exudation, evidently consisting of coagulated fibrin, could be traced between the cells of this zone. This exudation could be distinguished from the network of the central zone by its much greater fineness. It was never present in great amount, was not seen in all the sections, and was not present in the entire extent of the third zone in a single specimen. The boundary of this zone was not sharply defined from the second zone, nor from the adjacent liver tissue. The normal arrangement of the liver cells was gradually lost in the third zone; the liver cells could, to be sure,

be followed for some distance into the third zone, becoming, however, gradually smaller and less distinct. Occasionally, also, isolated liver cells were to be seen between the elements of this zone. A necrosis of the liver cells could never be detected, although they were sometimes compressed. Usually no definite proliferation was present, and karyokinetic figures in the liver cells could be discovered only in rare instances. In the liver tissue adjoining the third zone, the capillaries were enlarged and filled with cells similar to those of the third zone. Whether the cells of the latter zone are derivatives of the liver cells (which is rendered not improbable by the discovery of occasional karyokinetic figures), or whether they originate from a proliferation of the cells of the stroma and blood-vessels, could not be definitely determined.

It was apparent that the larger liver nodules had their origin in the connective tissue, and in many of them the lumen of a vessel could be perceived in the centre.

Kidney. — The microscopic examination of the umbilicated nodules situated on the surface of the kidney, afforded most interesting results. Serial sections showed that the umbilication was most marked in the sections through the centre of the nodules, and it was seen in all the sections, that at the periphery of the nodule, the umbilication was separated from the normal surface of the kidney by a prominent elevation of the surface, in other words, by a kind of wall. (Fig. 2, d.) Three zones, similar in character to those in the liver, could be distinguished in the kidney also. In the umbilicated nodules situated on the surface, the central zone exhibited a network, which was much better developed than that in the liver nodules, and which extended through almost the entire nodule. Here, too, it was most prominent in the sections from the centre, where the similarity to the network of an umbilicated small-pox lesion of the skin was very striking. (Fig. 2, a.) Frequently no urinary tubules could be distinguished in the central zone; in the places where they could be seen, however, they were usually altered, appearing either compressed, with shrunken epithelium, or with the nuclei of the epithelial cells faintly or not at all stained. A connection could be traced between the trabeculae of the network, and these partially or wholly necrotic cells. The Malpighian bodies could usually be dis-

tinguished in the area of the central zone, although the nuclei of many of the endothelial cells were no longer visible, or the cells themselves were transformed into amorphous masses, which were connected with the rest of the network. The capillary loops were, as a rule, filled with red blood globules, which were also collected in the interstices of the entire network, affording an explanation of the red color of the centre of the nodule, seen with the naked eye. The boundary line of the central zone was a zigzag one, as could be seen even macroscopically. The second zone corresponded to that in the liver nodules, and consisted in like manner of small, round cells and granular detritus, thickly heaped together and deeply stained, between which no urinary tubules could be distinguished. Occasionally a Malpighian body, filled with cells, could be made out. Frequently the outer zone was simply indicated by a gradual transition of the second zone into the surrounding kidney tissue. This outer zone was never so broad as in the liver nodules, but where it was best developed it consisted of cells similar to those in the corresponding zone of the latter, and in like manner contained in places a finely fibrillar, fibrinous exudation.

Lungs. — The nodules in the lungs also exhibited three zones, which could be distinguished with the naked eye in the stained preparations. In the inner zone the tissue was necrotic and at times transformed into a network similar to that described in the liver and kidney nodules. The network was here also most plainly shown in the central portions of the nodules, but was not so well developed as in the kidney. Many red blood globules, as well as finely granular masses, were collected in the interstices of the network, a sufficient explanation of the red color of the centre of these nodules. The alveolar structure was only suggested within the necrotic zone. In the alveoli that were still intact, and in their walls, only non-nucleated cells were, as a rule, to be seen. The second zone was exactly similar to that in the other nodules, the normal lung tissue being completely obliterated. The third zone proved to be much broader in the nodules in the lungs than in the other organs, and exhibited the appearances of a desquamative pneumonia; *i.e.*, the alveoli were filled with proliferated epithelium, and the alveolar walls infiltrated with cells. Occasionally, however, an alveolus was found in the vicinity of the second zone, containing the very same cells as the second zone

itself. No appearance of a fibrinous exudation could be detected here.

Numerous sections from the liver, kidneys, and lungs were examined for micro-organisms with the following result:—

Numerous micrococci arranged in chains were found in the sections from the liver, situated chiefly in the liver capillaries. *Micrococci were never found in the nodules themselves*, nor were they more numerous in the vicinity of the nodules than in the other parts of the liver. The micrococci could be stained by Gram's method, but were best seen, when (after treatment with the iodine solution) the sections were simply passed through alcohol, and decolorized chiefly in oil of cloves, several times renewed. They were also very beautifully stained by decolorizing with aniline oil, as lately recommended by Weigert.¹

Very few micrococci were found in the sections from the lung and kidney. Those seen were arranged in chains, and were chiefly within the blood-vessels. In many sections they were wholly wanting. *In these organs, also, all attempts to demonstrate micrococci or other forms of bacteria in the nodules themselves* were unsuccessful, although the various methods of staining were tried.

The cultures show that the micrococcus found outside the nodules was the *Streptococcus pyogenes*. The fact that the *Streptococcus pyogenes* was cultivated from a nodule of the liver, is not inconsistent with the microscopic examination, by which no micrococci were found in the nodules; a simple explanation being, that, on cutting into the nodules, the adjacent liver tissue was also incised, by which means the *Streptococcus* that was present in the latter gained entrance into the cultures.

As to the pathological significance of these nodules, it is evident, in the first place, that we are not dealing with syphilis nor with tubercle. There is, however, a striking similarity between the structure of these nodules and that of the variola pustule. We have in both a peculiar kind of necrosis in the centre, which progresses to form non-nucleated, irregular masses, and, further, a network formed from the necrotic cells.

This necrosis, found in the centre of the nodule, is evidently to be considered the primary change, and is to be referred to the

¹ Fortschritte der Medicin. 1887. Nr. 8.

action of the variola poison. Besides this necrosis, we find in the nodules, as well as in the skin efflorescences, the appearances of a reactionary inflammation, which is manifested in the skin lesion by a proliferation of the epidermal cells, and by the appearance of suppuration, but in the nodules by the formation of the small cells of the second zone, similar to pus corpuscles, which are partially killed by the continuous action of the variola poison. This inflammation is also characterized by the deposition of a fibrinous exudation in the third zone, and by the appearance of the cell elements of this zone, which are derived either from a proliferation of the cells of the stroma and vessels, from a proliferation of parenchymatous cells, or from both together. It is apparent, therefore, that in both lesions, in the skin efflorescences and in the nodules of the internal organs, the essential changes are the same. A similarity between the two products is seen even in the umbilication. We were able, in those nodules that lay on the surface of the lung and kidney, to demonstrate a pronounced umbilication, apparently produced in a similar way to the umbilication of the skin lesion. Different theories have been advanced as to the method of formation of the umbilication in the small-pox pustule of the skin, of which that of Weigert seems to me most plausible. Weigert regards the umbilication as caused by a growth of cells at the periphery of the lesion, the centre being held down by firm bands of tissue, which have undergone a diphtheroid necrosis. The umbilication of the nodules in the internal organs is best explained by this theory. Here, too, we have a strong network in the centre, which binds the surface of the nodule to the base, and counteracts the tendency of the exudation to force up the surface, while at the periphery in the area of the second and third zones, a projection of the surface is caused by the proliferating cells.

Taking into account, therefore, the evidence that has been adduced, I think we are justified in regarding these nodules in the liver, kidneys and lungs, as true small-pox efflorescences of the internal organs.

The fact alone, that micrococci were never found *in* the nodules, is opposed to the assumption that they bear a causal relation to them, as well as the fact that these micrococci were present in the kidneys and in the lungs much more sparingly than in the liver,

although numerous nodules were found in the former organs. Moreover, these micrococci were shown by cultures to be the *Streptococcus pyogenes*, and it cannot be supposed that this micrococcus represents the poison of small-pox. While the specific virus of small-pox has not yet been discovered, we know that the organism of a patient ill with variola affords a very favorable soil for the development of other pathogenetic bacteria. For example, the *Staphylococcus pyogenes aureus* or *albus* has been repeatedly found in the contents of small-pox pustules. Professor Weichselbaum informed me that he could not only confirm these observations, but that in two cases of hæmorrhagic small-pox that had terminated fatally on the seventh day of the disease, *i.e.*, at a time when papules even were hardly to be seen on the skin, he had cultivated the *Streptococcus pyogenes* from the skin lesion, as well as from the blood and from the internal organs. It is probable that many of the complications that arise during the course of variola are to be ascribed to this secondary inroad of the *Staphylococcus* or *Streptococcus*, while the origin of the specific products of small-pox, *i.e.*, the efflorescences on the skin and mucous membranes, is quite independent of these micro-organisms. We regard, therefore, the absence of the *Streptococcus pyogenes* in the nodules, as a further proof that the latter are to be regarded as specific products of the yet unknown poison of small-pox, and as analogous to the lesions of the skin. Since no micrococci could be found in these nodules, we may assume that they originated before the immigration of the *Streptococcus pyogenes*. The *Streptococcus* could not afterward penetrate into the nodules easily, at all events, not by way of the circulation, since the latter had come to a stand-still in consequence of the necrosis in the centre.

The appearances in the internal organs, described by Weigert as resembling the skin efflorescences, demand a few words. As regards the small microscopic foci, it seems probable that they were not analogous to the efflorescences on the skin. They exhibited, in the first place, simply a necrosis, consisting in a disappearance of the cell nuclei, while all the other changes that appear in the skin lesion were wanting here. Moreover, we know to-day that such a necrosis can be caused by different pathogenetic micro-organisms, and in particular by the *Staphylococcus pyogenes*

aureus, and by the *Streptococcus pyogenes*. As the centre of the foci seen by Weigert constantly contained blood-vessels filled with micrococci, and as it is most probable, according to the belief of to-day, that these micrococci were none other than *Staphylococcus* or *Streptococcus*, and in any case a secondary manifestation, we are justified in concluding that these foci were not specific products of the variola poison, but the result of the action of a secondary incursion of micrococci. It is probable, however, that in one case described by Weigert, in which miliary nodules, visible macroscopically, were seen in the liver, the lesions were analogous to the skin eruption. In this case the cells were transformed into glistening, amorphous masses, and between them lay small, intensely stained granules; in other words, elements similar to those found in the second zone of our nodules, and also in the skin efflorescences. From the fact that in the centre of these nodules the blood-vessels were filled with micrococci, the possibility that in this case also the changes were due to a secondary inroad of micro-organisms, cannot be wholly excluded.

In order to form an opinion with regard to the changes in the testicles in variola, especially the nodules found by Chiari, it was deemed necessary to examine personally a number of cases microscopically. The cases were placed at my disposal by the kindness of Professor Weichselbaum, and were six in number.

CASES 1 AND 2.—*Variola hæmorrhagica*. In each instance the disease had terminated fatally on the seventh day. In the first case the age was $4\frac{1}{2}$ years; in the second case, 6 months. Nothing abnormal could be detected in the testicles with the naked eye. Very numerous sections through different parts of the organs were made, stained, and carefully examined microscopically, but with the exception of a few small hæmorrhages, no pathological appearances could be found.

The remaining four cases yielded a positive result. The microscopic appearances will be described at the end.

CASE 3.—*Variola confluens in stadio exsiccationis*. Boy, 7 years of age. Death on the 17th day of the disease. In the testicles a number of yellowish foci, from the size of a millet-seed to that of a hemp-seed. Also suppuration of the elbow joint, and of the periarticular connective tissue.

CASE 4.—*Variola confluens in stadio exsiccationis*. Man, 22

years of age. Death on the 17th day of the disease. In both testicles numerous yellowish nodules, the size of a hemp-seed.

CASE 5.—*Variola confluens*. Man, 29 years of age. Duration of disease, 24 days. In the testicles a few yellowish nodules, somewhat smaller than those of the preceding case.

CASE 6.—*Variola confluens in stadio exsiccationis*. Man, 29 years. A pleuritic exudation, and metastatic abscesses in the lungs. In the testicles no nodules detected with the naked eye.

In the 3d, 4th, and 5th cases many nodules were seen after the sections had been stained which were not visible before. In the 4th case the nodules were very numerous, and often confluent, forming irregular foci. In the 6th case no abnormal appearances could be detected until the sections were stained, when small, dark points were seen, occurring, however, in only a few preparations from a large number of sections.

The microscopic appearance of these foci agreed in the main with the description of Chiari. The inner necrotic zone, and the second zone of small-celled infiltration, were found in all cases to agree with Chiari's description. A third zone, similar to that described as occurring in the nodules of the liver, lung, and kidney of our first case, could frequently, but not always, be seen in the foci in the testicles. It was never sharply bounded from the second zone, and was gradually lost in the surrounding normal tissue. It consisted chiefly of large cells, while small cells with deeply stained nuclei were to be seen, similar to those in the second zone, but less numerous. A finely fibrillar exudation was very frequently found between the cells, extending oftentimes throughout the whole extent of the third zone, but sometimes present only in isolated portions. Sometimes the seminal tubules for some distance from the second zone had undergone a partial necrosis.

Are these foci really analogous to the skin efflorescences, as Chiari assumes? It cannot be denied that their microscopic appearances seem to favor this view. The foci consisted of three zones, as did the nodules of the internal organs in our first case, and moreover, the structure of these foci corresponded in general with that of the latter. Only one point of difference was observed, and that was that the inner zone of the testicle foci never presented that diphtheroid network that could be so plainly demon-

strated in many sections from the nodules of the internal organs, although in a very few sections it seemed to be suggested.

Although the nodules in the testicles were most carefully examined, and the various methods of staining attempted, no micrococci or bacteria of any description could be detected, a point in evidence in favor of their specific nature. Had the micrococci which Weigert demonstrated in the non-nucleated foci of the internal organs, and also in the skin lesion (probably the *Streptococcus* or *Staphylococcus pyogenes*), been present constantly or very frequently in the testicle foci, even then their specific nature would have been, for the reasons mentioned above, very improbable. The fact that Chiari found micrococci in the foci, is not opposed to this view. From fifteen cases Chiari was able to demonstrate micrococci in two only; which renders the assumption, that the micrococci were in these cases a secondary element, much more probable than that a causal relation existed between these micrococci and the foci in the testicles, apart from the fact that these micrococci surely do not represent the poison of small-pox. A final decision of this question will not, however, be possible, until we have some definite knowledge of the contagium of small-pox.

It seems probable that these lesions in the internal organs are more common than has been hitherto supposed. At all events, in the case of the testicles, the observations of Chiari, taken in connection with the cases above described, prove that their appearance in these organs is a most frequent occurrence. The importance of recognizing these changes is found in the fact that they afford an additional source of etiological investigation, as Chiari observes; a source the more hopeful, inasmuch as their position, in the internal organs, renders them much less liable to secondary changes than the more exposed skin lesions.

Before concluding, I wish to give a short account of some studies of the manifestations of small-pox on the skin and mucous membranes. The material was obtained (through the kindness of Professor Weichselbaum) from the small-pox department of the Rudolph Hospital, in Vienna, in every case within a few hours after death, and in two of them immediately after. In all, nine cases were examined, and from each of these a large number of specimens were taken. The material was hardened, partly in

alcohol, partly in Müller's fluid, and partly in Flemming's solution, and the pieces were cut in serial sections through the entire lesion. The diphtheroid degeneration described by Weigert was found in every specimen, always most marked in the centre of the lesion, where the lowest layer of rete cells was transformed into glistening, compact masses, the boundaries of the separate cells were with difficulty distinguished, and the nuclei could be differentiated by none of the ordinary methods of staining. The connection between these diphtheroid masses and the meshes of the overlying network could be plainly traced, and where an umbilication existed, diphtheroid bands, evidently resulting from a like necrosis of the middle and upper layers of the rete, could be seen connecting the epidermis with the masses in the lower rete.

Similar appearances were found in the efflorescences on the mucous membrane of the larynx and pharynx.

Several cases were examined for nuclear division. The pieces were excised immediately after death, and hardened partly in Flemming's solution and partly in absolute alcohol. The figures seen, after staining with safranine and dahlia violet, were in every case very few in number. Their position, however, was constant. At the side of every well-developed efflorescence, in the middle and upper layers of the rete, the epithelial cells are swollen, and often provided with from two to four nuclei. In this region of proliferating cells, and here only, were the figures found. In many sections examined, simply an indication of karyokinetic figures could be traced, or sometimes irregular forms. Occasionally, a typical convoluted or stellate figure was seen. In the other portions of the lesion the nuclei showed no signs of division.

EXPLANATION OF THE FIGURES.

Fig. 1. Nodule from the liver, of which only one-half is represented. Reichert obj. 7, oc. 3.

a— Central necrotic zone; the network is not distinctly shown by the drawing.

b— Second zone, with infiltration of small cells.

c— Third or outer zone, with occasional threads of fibrin between the cells.

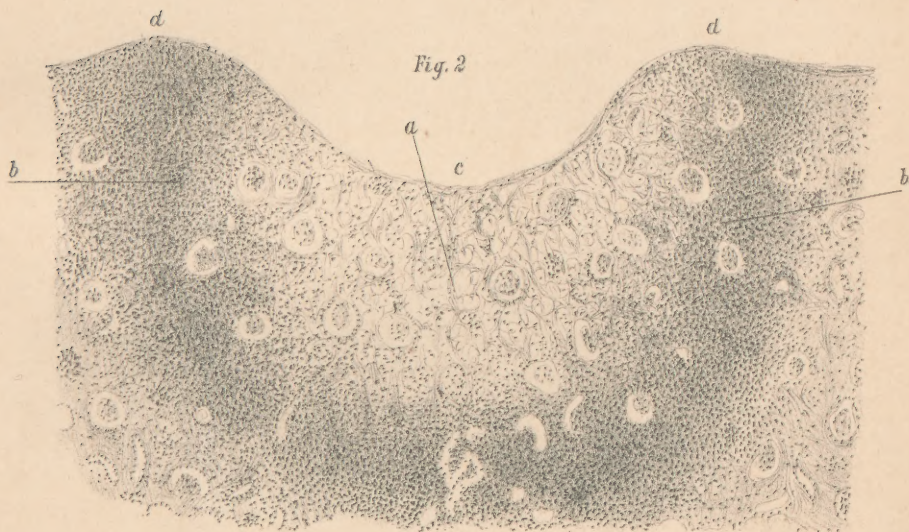
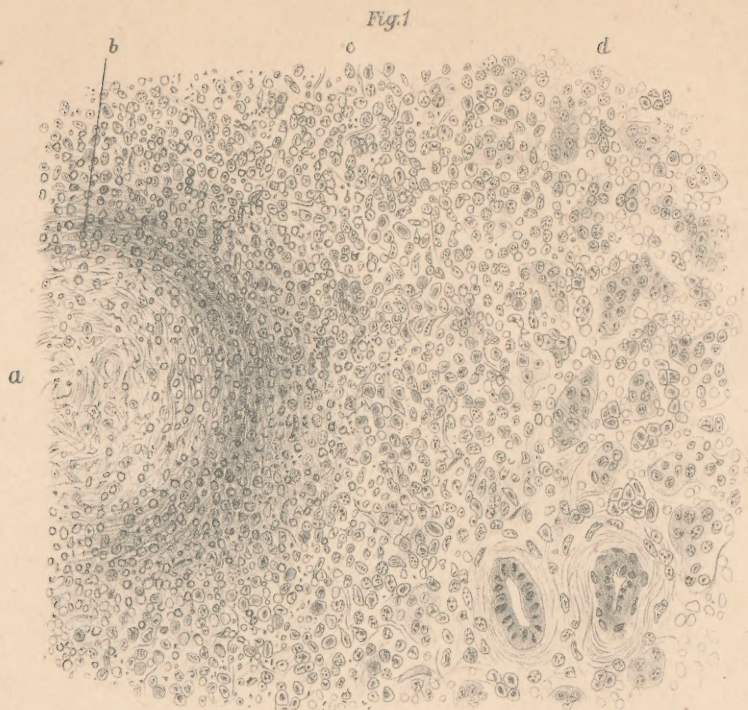
Fig. 2. Nodule from the kidney, with umbilication. Reichert obj. 4, oc. 3.

a— Network of the central zone.

b— Second zone.

c— Umbilication.

d— Wall.



Bowen: Vorkommen pockenähnliche Gebilde in inneren Organ.

Lith. Anst. v. Th. Bannwarth, Wien.

